Respiratory Medicine (2004) **98**, 1093–1101

respiratoryMEDICINE

Antibiotic prescribing rates in the US ambulatory care setting for patients diagnosed with influenza, 1997–2001

Gabrielle Ciesla[a,*], Shelah Leader[a], Jeffrey Stoddard[b]

[a]*MedImmune, Inc., One MedImmune Way, Gaithersburg, MD 20878, USA*
[b]*MedImmune Vaccines, Inc., One MedImmune Way, Gaithersburg, MD 20878, USA*

Received 18 December 2003; accepted 22 March 2004

KEYWORDS
Antibiotics;
Influenza;
Cost

Summary To document the rate and cost of antibiotic prescribing for patients diagnosed only with influenza during US ambulatory care visits. Federal survey data for 1997–2001 were used to estimate outpatient trends for all patients and healthy people age 5–49 years. Cost estimates were based on Medicare payments and Red Book average wholesale prices in 2003. Antibiotic prescribing for influenza is widespread; 38% of visits led to an antibiotic prescription of which one-third were for broad spectrum antibiotics. Inappropriate antibiotics cost $18.5 million annually and may contribute to resistance. Increased vaccination rates and viral testing could reduce these trends.

Introduction

A series of large-scale studies has demonstrated that antibiotics are commonly prescribed for colds, upper respiratory tract infections (URIs), and bronchitis among both children and adults. Such usage constitutes a large percentage of the total antibiotic prescribing which occurs in ambulatory practice, and is generally reflective of inappropriate treatment for infections of primarily viral etiology.[1–3] This inappropriate use of antibiotics has contributed to the growing public health problem of antibiotic resistance among pathogenic bacteria.[4,5] In addition, widespread antibiotic overuse has been shown to carry with it substantial cost implications.[6,7] Recent reports indicate that rates of inappropriate antibiotic prescribing for colds, URIs and bronchitis peaked in the mid-1990s and may be decreasing modestly, although they remain at unacceptably high levels.[8–12]

Most prior analyses of inappropriate antibiotic use in ambulatory care have examined diagnostic codes characterized by clinical terminology suggestive of a viral etiology. No studies, to our knowledge, have examined rates of antibiotic prescribing in ambulatory care for cases in which the sole recorded diagnosis is influenza. Influenza, a viral respiratory illness, is known to present with a clinical picture characterized by febrile respiratory illness in which symptoms are often severe and of a systemic nature.[13] Notwithstanding the severity of influenza, the inherent viral etiology of the diagnosis by definition precludes appropriate use of antibiotics in those cases in which it is the sole diagnosis. We therefore undertook this study specifically to ascertain the rate and associated

*Corresponding author. Tel.: +1-301-398-4757; fax: +1-301-398-9757.
E-mail address: cieslag@medimmune.com (G. Ciesla).

0954-6111/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.rmed.2004.03.021

cost of antibiotic prescribing in ambulatory practice for patients diagnosed only with influenza. By restricting cases to those for which influenza is the sole recorded diagnosis, judgment as to the appropriateness of antibiotic prescribing is made even less subjective compared to prior analytic approaches.

We focus our analysis on patients between the ages of 5 years and 49 years for three reasons. First, most prior studies of disease burden attributable to influenza have historically focused on groups at high risk of complications from influenza (such as the elderly and young children) while comparatively few studies have looked at influenza-associated disease burden within this age range; thus a gap in the epidemiologic literature exists for this population subgroup. Second, new advances in influenza prevention target this age range.[14] Lastly, within the specific subgroup of 5–49 year olds, there is a diminished likelihood that clinicians' concerns about possible complications (such as bacterial superinfections) would influence therapeutic decision-making. For all of these reasons, our research question addresses a novel and unaddressed area that is relevant within the current context of influenza prevention, diagnosis and treatment.

Methods

The National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Ambulatory Medical Care Survey (NHAMCS) data were used for this analysis. These ambulatory medical care datasets are provided by the National Center for Health Statistics (NCHS), a subdivision of the US Centers for Disease Control and Prevention. The datasets are free for public use and can be downloaded from the NCHS website (http://www.cdc.gov/nchs/about/major/ahcd/ahcd1.htm).

Both the NAMCS and NHAMCS are national visit-based surveys designed to collect information annually about the provision and utilization of ambulatory medical care services. The NAMCS is based on visits to nonfederally employed office-based physicians. The NHAMCS is collected on visits to the emergency and outpatient departments of noninstitutional general and short-stay hospitals, exclusive of federal, military, and Veterans Administration hospitals, located in the 50 states and the District of Columbia.

The NAMCS survey is completed by physicians and their staff, whereas the NHAMCS is completed by hospital staff. The same data form is used to collect information in the office and outpatient department settings. A different form is used to capture information in the emergency department. Both forms contain information about the visit including demographic data, up to three diagnoses and up to six medications ordered, supplied, administered or continued. Free text diagnoses and medications are coded by NCHS to International Classification of Disease (ICD-9-CM) codes and NCHS drug codes, respectively.

The NAMCS uses a three-stage probability sample design. The three stages include probability samples of geographically defined areas (primary sampling units or PSUs), physician practices within these areas and patient visits within practices. The NHAMCS uses a four-stage probability design with samples of geographically defined areas, hospitals within these areas, clinics within hospitals, and patient visits within clinics.

National estimates were produced by weighting the NAMCS and NHAMCS samples using the patient visit weights provided. Estimates reported in this analysis are based on sample cases of 30 or more and have relative standard errors (RSE) less than 30%. Standard errors were used to calculate the 95% confidence intervals (CI) around the estimates. The SURVEYMEANS procedure in SAS version 8.2 (Cary, NC) was used to calculate estimates of population totals and means with estimates of variances and confidence limits.[15] When appropriate, the DOMAIN statement was used in the SURVEYMEANS procedure to perform statistically valid subpopulation analyses.

The NAMCS and NHAMCS data from 1997 to 2001 were merged with each other for this analysis. Combining the datasets creates a larger sample and allows for analyses across multiple settings. These 5 years of data could be combined because the questions of interest were asked consistently over the years.[16] SAS version 8.2 software was used for all statistical analyses. Microsoft Excel was used to calculate population-based visit rates using post-censal estimates of noninstutionalized civilian population provided by the US Bureau of Census (http://eire.census.gov/popest/data/national/asro_detail.php).

Inclusion criteria

Visits by individuals age 5–49 years with an influenza diagnosis were identified in both the NAMCS and NHAMCS data. Up to three diagnoses may be recorded for each visit. Diagnoses written as free text are coded by NCHS staff as ICD-9-CM

codes. The following ICD-9-CM codes were used to identify influenza for this analysis:

- 487.0 Influenza with pneumonia
- 487.1 Influenza with other respiratory manifestations
- 487.8 Influenza with other manifestations

To reduce the number of individuals with comorbid conditions, the analysis cohort was limited to subjects who had only a primary diagnosis of influenza and no secondary diagnoses.

Identification and classification of antibiotics

Prescribed drugs are recorded in the NAMCS and NHAMCS by trade name, generic name, desired therapeutic effect or by ingredient names for combination products. These free text responses are recoded using unique NCHS-assigned medication codes. Medications were queried using the Ambulatory Care Drug Database System (http://www2.cdc.gov/drugs) provided by NCHS to obtain drug name, generic name and therapeutic class. Medications assigned to the following NCHS-assigned therapeutic classes were identified as antibiotics: penicillins (346); cephalosporins (347); erythromycins, lincosamides and macrolides (348); polymyxins (349); tetracyclines (350); chloramphenicol and derivatives (351); aminoglycosides (352); sulfonamides and trimethoprim (353); and quinolones and derivatives (357). Antibiotics were further classified as broad- or narrow-spectrum based on methods used in a previous study[12] and expert opinion (Table 1).

Visit costs

Three current procedural terminology (CPT) codes matching the expected level of care and reported patient status (new or established) were selected to represent the professional services likely rendered at an influenza-related ambulatory care visit. CPT 2003 Professional Edition was used to define CPT codes (Table 2). The selected CPT codes were assigned to each visit by care setting and patient status. Patient status was not reported for emergency department visits.

The Medicare national average allowance (NAA) for each CPT code was calculated using the National Fee Schedule Relative Value File provided by the Centers for Medicare and Medicaid Services (http://cms.hhs.gov/providers/pufdownload/rvudown.asp). The NAA is the average Medicare payment calculated by summing the relative value units (RVUs) for a specific procedure and multiplying the sum by $36.7856, the 2003 Medicare conversion factor (CF). Geographic practice cost indices (GPCI) are not needed in the NAA calculation since the average GPCI is 1.0 (Table 2).

Drug costs

Since prescribed dosing and duration of therapy are not available in the survey data, we used the recommended doses listed in the Physicians' Desk Reference® (PDR) Electronic Library™ for each antibiotic recorded.[17] Duration of therapy ranged from a single dose to 10 days. Antibiotics were then queried in the Medical Economics RED BOOK™

Table 1 Antibiotics classified as broad- or narrow-spectrum.

Broad-spectrum	Narrow-spectrum
Amoxicillin-clavulanate potassium	Amoxicillin
Azithromycin	Ampicillin
Cefaclor	Cefadroxil
Cefotaxime	Cephalexin
Cefprozil	Cephapirin
Ceftizoxime	Cephradine
Ceftriaxone	Cyclacillin*
Cefuroxime axetil	Erythromycin
Ciprofloxacin	Erythromycin ethylsuccinate
Clarithromycin	Erythromycin-sulfisoxazole
Doxycycline	Penicillin*
Levofloxacin	Penicillin G
Loracarbef	Penicillin V
Tetracycline	Sulfamethoxazole/trimethoprim

*Discontinued product or vague description provided in NCHS Ambulatory Care Drug Database System. Cost estimates for penicillin V were used.

Table 2 CPT codes, descriptions and Medicare national average allowance (USD, 2003).

CPT code	CPT description	NAA (USD, 2003)
99202	Office or other outpatient visit for the evaluation and management of a *new* patient. Usually the presenting problem(s) are of low to moderate severity. Physicians typically spend 20 min face-to-face with the patient and/or family	$62.54
99213	Office or other outpatient visit for the evaluation and management of an *established* patient. Usually, the presenting problem(s) are of low to moderate severity. Physicians typically spend 15 min face-to-face with the patient and/or family.	$51.13
99283	Emergency department visit for the evaluation and management of a patient. Usually, the presenting problem(s) are of moderate severity.	$60.33

Source: CPT codes and descriptions were obtained from the CPT 2003 Professional Edition (American Medical Association, 2002). NAAs were calculated from the Medicare National Fee Schedule.

database.[18] This database provides information about average wholesale prices (AWP) for drugs, direct prices, federal upper limit prices and complete package information including dosage form, route of administration, strength and size. AWPs obtained from RED BOOK™ were used to derive a cost for each antibiotic prescription, expressed as 2003 US dollars. The April 2003 release of the RED BOOK™ was used.

The recommended standard dose, duration of therapy and average wholesale price were used to calculate a drug cost for each antibiotic prescribed. Individual drug costs were averaged by group to create an unweighted mean cost for broad- and narrow-spectrum antibiotics. The unweighted mean cost was assigned to each visit based on the group of antibiotics prescribed. Then the unweighted mean group costs were weighted to produce national estimates of total antibiotic costs. Drug costing assumes that recorded antibiotic prescriptions were filled.

Results

All ages

An estimated 14.4 million (95% CI:12.1–16.8) ambulatory care visits in the US were made by children and adults of all ages for a primary diagnosis of influenza over a 5-year period, 1997–2001. Seventy-five percent of these visits were for a primary diagnosis of influenza with no secondary diagnoses (Table 3). The cumulative visit rate to physician offices, hospital outpatient departments and hospital emergency departments was 7.9/1000 persons (95% CI:6.5/1000–9.4/1000). Annual visit rates ranged from 5.2/1000 persons (95% CI:4.2/1000–6.2/1000) to 12.7/1000 persons (95% CI:8.0/1000–17.3/1000).

Ages 5–49 years

An estimated 8.3 million (95% CI:6.6–10.0) ambulatory care visits in the US were made by children and adults age 5–49 years for a primary diagnosis of influenza over a 5-year period, 1997–2001. Seventy-eight percent of these visits were for a primary diagnosis of influenza with no secondary diagnoses (Table 3). The visit rate for patients age 5–49 years over the 5-year period to physician offices, hospital outpatient departments and hospital emergency departments was 7.4/1000 persons (95% CI: 5.6/1000–9.1/1000). Annual visit rates ranged from 3.9/1000 persons (95% CI: 2.6/1000–5.2/1000) to 12.8/1000 persons (95% CI: 6.5/1000–19.2/1000). The average number of visits per year was 1.3 million.

The cumulative visit rate for children age 5–17 years was higher than the visit rate for adults age 18–49 years: 8.5/1000 persons (95% CI: 5.6/1000–11.3/1000) and 6.9/1000 persons (95% CI: 5.1/1000–8.7/1000), respectively. The visit rate for children age 5–17 years in the office-based physician setting was 7.5/1000 persons (95% CI: 5.3/1000–9.7/1000) compared to 5.7/1000 persons (95% CI: 4.1/1000–7.3/1000) for adults age 18–49 years (Table 4).

All subsequent analyses were performed on the cohort of children and adults age 5–49 years with a primary diagnosis of influenza and no secondary diagnoses coded for the visit.

Females made 56.8% of all ambulatory care visits for influenza during the 5-year period. The overall visit rate for all females was 8.3/1000 (95% CI: 6.5/1000–10.2/1000) compared to 6.4/1000 (95% CI:

Table 3 Frequency of influenza visits in the ambulatory care setting, 1997–2001.

Characteristic	All ages			Age 5–49 years			
	Estimate	% of visits	Visit rate per 1000*	Estimate	% of visits	% of all influenza visits	Visit rate per 1000*
All visits with an influenza dx	16 277 509	100.0	8.7	9 364 429	100.0	57.5	7.6
All visits with a 1° dx of influenza	14 414 833	88.6	7.7	8 336 613	89.0	57.8	6.7
Other 2° dx(s)	3 675 323	25.5	2.0	1 761 235	21.1	47.9	1.4
No other 2° dx(s)	10 739 510	74.5	5.7	6 575 378	78.9	61.2	5.3
All visits with a 2° dx of influenza	1 862 676	11.4	1.0	1 027 816	11.0	55.2	0.8

Source: CDC's National Center for Health Statistics. Public use files (micro-data), National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey, 1997–2001.
*Based on US Bureau of the Census monthly postcensal estimates of the civilian noninstitutionalized population of the United States as of July 1 each year.

Table 4 Estimated numbers of ambulatory care visits, distribution and visit rates in the US by children and adults age 5–49 years with a sole diagnosis of influenza, 1997–2001.

Setting	5–17 years	18–49 years	5–49 years
Physician office			
Number of visits	1 928 562	3 632 176	5 560 738
Percent distribution	88.0%	82.9%	84.6%
Visit rate per 1000* (95% CI)	7.5 (5.3, 9.7)	5.7 (4.1, 7.3)	6.2 (4.4, 8.1)
Hospital outpatient department			
Number of visits	105 155	214 903	320 058
Percent distribution	4.8%	4.9%	4.9%
Visit rate per 1000* (95% CI)	0.4 (0.2, 0.6)	0.3 (0.2, 0.5)	0.4 (0.2, 0.5)
Hospital emergency department			
Number of visits	158 547	536 035	694 582
Percent distribution	7.2%	12.2%	10.6%
Visit rate per 1000* (95% CI)	0.6 (0.4, 0.9)	0.8 (0.7, 1.0)	0.8 (0.6, 1.0)
Combined settings			
Number of visits	2 192 264	4 383 114	6 575 378
Percent distribution	33.3%	66.7%	100.0%
Visit rate per 1000*	8.5 (5.6, 11.3)	6.9 (5.1, 8.7)	7.4 (5.6, 9.1)

Source: CDC's National Center for Health Statistics. Public use files (micro-data), National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey, 1997–2001.
*Based on US Bureau of the Census monthly postcensal estimates of the civilian noninstitutionalized population of the United States as of July 1 each year.

4.1/1000–8.7/1000) for males. Patients were predominantly white (84.3%) with a visit rate of 7.7/1000 (95% CI: 5.8/1000–9.7/1000). Blacks made 13.8% (7.5/1000; 95% CI: 3.0/1000–12.0/1000) of visits and other races made the remaining 1.9% of visits. The three most common expected sources of payment were private insurance, Medicaid and self-pay. Over the 5-year period, private insurance accounted for 63.5%, Medicaid 15.7% and self-pay 13.2% of the expected payment sources.

Data from three ambulatory care settings were combined for this study: office-based physicians, hospital outpatient departments and hospital emergency departments. Visits to office-based physicians accounted for 85% of all visits made by this age cohort over the 5-year period. Nearly 11% of visits were made to hospital emergency rooms and the remaining 4.9% were made to hospital outpatient departments. The clinic type is available for the 320 058 visits (95% CI: 188 499–451 617)

Table 5 Estimated number of antibiotic prescriptions reported at ambulatory care visits by children and adults age 5–49 years with a sole diagnosis of influenza, 1997–2001.

	No. visits	% visits	Visit rate per 1000* (95% CI)
All Visits	6 575 378	100.0	7.4 (5.6, 9.1)
Antibiotics prescribed at visit			
Yes	2 493 781	37.9	2.8 (1.4, 4.1)
No	4 081 597	62.1	4.6 (3.5, 5.6)
	No. antibiotics†	% antibiotics	Visit rate per 1000* (95% CI)
Antibiotic classification			
Total antibiotics prescribed	2 590 085	100.0	2.9 (1.4, 4.4)
Broad-spectrum	988 406	38.2	1.1 (0.5, 1.8)
Narrow-spectrum	1 601 679	61.8	1.8 (0.8, 2.8)

Source: CDC's National Center for Health Statistics. Public Use Files (micro-data), National Ambulatory Health Care Survey and National Hospital Ambulatory Medical Care Survey, 1997–2001.
*Based on US Bureau of the Census monthly postcensal estimates of the civilian noninstitutionalized population of the United States as of July 1 each year.
†More than one antibiotic may have been prescribed at a visit.

made to hospital outpatient departments. Nearly 85% of all outpatient department visits were made to a general medicine department. Visits were also made to surgery and pediatric clinics. Physician specialty is available for the 5.5 million visits (95% CI: 3.9–7.1) made to office-based physicians. General/family practice physicians accounted for 53% or 2.9 million visits. The remainder of visits were made to internists, pediatricians, neurologists, otolaryngologists and other specialists.

The CDC reports that the peak of influenza season can occur anywhere between December and March (http://www.cdc.gov/flu/about/disease.htm). The peak months for influenza visits in this 5-year study were February (33.9%), January (25.2%) and March (12.6%). The observed pattern of visits reported in the NCHS surveys is consistent with the CDC's tracking of the seasonality of influenza.

Antibiotic prescribing rates and cost (USD, 2003)

During the 5-year period studied, antibiotics were prescribed during 38% of all ambulatory visits for influenza. Of the nearly 2.6 million antibiotic prescriptions (95% CI: 1.3–3.9) recorded during these encounters, 38.2% were for a broad-spectrum antibiotic and 61.8% were for a narrow-spectrum antibiotic (Table 5).

The estimated aggregate cost for the 988 406 (95% CI: 412 473 to 1.6 million) broad-spectrum antibiotics prescribed was nearly $59 million dollars (95% CI: $24.5–$93.4 million) (USD, 2003) over the 5-year period, an average of $11.8 million dollars per year. The estimated cost for the 1.6 million narrow-spectrum antibiotics prescribed was $33.9 million dollars (95% CI: $15.1–$52.8 million) over the 5-year period, an average of $6.8 million dollars per year. The total estimated antibiotic cost over the 5-year period was $92.9 million dollars (95% CI: $45.4–$140 million), an average of $18.6 million dollars per year. Broad-spectrum antibiotics were prescribed less frequently, but accounted for 63.5% of the total antibiotic cost (Table 6).

Total direct medical costs

Over 6.5 million (95% CI: 5.0–8.1) ambulatory care visits were made in the US by children and adults age 5–49 years from 1997 to 2001 for a primary diagnosis of influenza with no secondary diagnoses. The estimated cost for the physician visits aggregated over the 5-year period was $348 million dollars (95% CI: $269–$427), an average of $69.6 million dollars per year. The total estimated direct medical cost including physician payments and antibiotic costs for the 5-year study period was $441 million dollars (95% CI: $323 –$560) with antibiotics contributing more than 20% to the total direct medical cost (Table 6).

Discussion

This is the first effort to document the extent of antibiotic use during U.S. ambulatory visits with

Table 6 Estimated costs (USD, 2003) of physician visits and antibiotics prescribed for ambulatory care visits by children and adults age 5–49 years with a sole diagnosis of influenza, 1997–2001.

	No. visits	Mean	Median	5-year sum	Average annual cost
Visit cost	6 575 378	$52.95	$51.13	$348 191535	$ 69 638 307
Antibiotic costs	2 493 781	$35.87	$21.17	$ 92 905 499	$ 18 581 100
Broad-spectrum	977 946	$59.69	$59.69	$ 58 997 954	$ 11 799 591
Narrow-spectrum	1 515 835	$21.17	$21.17	$ 33 907 544	$ 6 781 509
Total direct medical cost (visit + antibiotic costs)	6 575 378	$67.08	$60.33	$441 097 033	$ 88 219 407

Source: CDC's National Center for Health Statistics. Public use files (micro-data). National Ambulatory Health Care Survey and National Hospital Ambulatory Medical Care Survey, 1997–2001.

only an influenza diagnosis. Our data show that over one-third of these visits resulted in an antibiotic prescription, and that over one-third of these prescriptions were for a broad-spectrum agent.

This high rate of antibiotic prescribing for patients diagnosed only with influenza is troubling in light of the documented increase in antibiotic resistance in the US.[19–21] Of even greater concern is the reported reliance on broad-spectrum antibiotics since they are more costly and should be reserved for clinically justified cases. Overuse or injudicious use of these agents can promote escalating antimicrobial resistance within both individual patients and populations.[22–26]

In order to more fully assess appropriateness, we examined the survey data for evidence of laboratory testing for the pathogen. Surprisingly, there were too few recorded cases of laboratory tests to be statistically reliable. This might suggest the need for ongoing educational efforts aimed at improving physicians' clinical diagnostic approaches when evaluating a patient presenting with a common viral infection.[13] Alternatively, it might reflect the relative lack of availability of accurate, reliable and affordable laboratory diagnostic methods for the rapid detection of influenza during the period over which the data were collected. It has become clear over the past 2 years that rapid diagnostic kits for the purpose of virologic confirmation of influenza are gaining favor in many outpatient facilities. Such increased testing, combined with enhanced prevention efforts, might ultimately result in reductions in inappropriate management of influenza.

To further explore the issue of appropriate treatment for influenza, we looked at the prescribing of antiviral drugs such as oseltamivir and amantadine. We observed that antiviral drugs were prescribed at 30% of visits; a lower rate than observed for antibiotics. This may reflect the relatively late stage of infection that occurs for many outpatient encounters in which influenza is diagnosed (at which point antiviral therapy is clinically ineffective).[27]

In an effort to identify potentially justifiable cases of antibiotic prescribing, we examined cases in which the sole diagnosis was influenza with pneumonia (ICD-9-CM 487.0). We found too few cases with this diagnosis to be statistically reliable. The cases accounted for 1.2% of the visits in which an antibiotic was prescribed. Ninety-eight percent of the visits had a sole, primary diagnosis of influenza with other respiratory manifestations. Since there is no broad diagnosis code for influenza, the ICD-9-CM code 487.1 is used to code influenza with other respiratory manifestations and influenza not otherwise specified. This is a limitation of the ICD-9-CM coding system and leads to potential misclassification bias in this analysis. We recognize that there may be cases where an antibiotic is warranted. However, we have attempted to define the best possible sample by excluding cases with any secondary diagnoses. Therefore, we conclude that the vast majority of antibiotic prescriptions were for uncomplicated cases of influenza.

Due to the small annual number of sample cases, and the limited span of the study, this study cannot address the issue of whether or not there is a trend toward decreased use of antibiotics to treat influenza.[12] Our findings are generally consistent with a recent report that 28% of managed care patients diagnosed only with influenza received an antibiotic.[28] Mean outpatient charges for these patients in 1997–1998 were $171.[28] A recent review of fluroquinolone use in a hospital outpatient department concluded that 33% of the time there was no evidence of an infection justifying the use of an antibiotic, much less a broad-spectrum agent. The authors concluded that inappropriate use of antibiotics in the ambulatory setting may be exacerbating antibiotic resistance.[29]

While the survey data used for this study do not capture the entire universe of ambulatory medical

care (e.g. community health centers and federal institutions such as VA outpatient clinics are excluded) they do permit nationally reliable estimates of care provided in most US mainstream ambulatory settings. An important limitation of this study is that diagnoses cannot be specifically associated with a particular drug, dose, or duration of therapy, and therefore the appropriateness of an antibiotic prescription cannot be assessed with absolute certainty. A further limitation of the data is that it is not known whether prescriptions were actually filled or taken as prescribed. Previous research has shown that up to one-fifth of all new prescriptions go unfilled.[30] Patient compliance cannot be assumed because patient and pharmacy records were not audited. However, the data accurately reflect physicians' self-reported actions during patient encounters.

In addition to increasing targeted education of physicians, both the visit rate for influenza related care and inappropriate use of antibiotics could be reduced by higher influenza vaccination rates and improved diagnostic virology and viral surveillance. Even among high-risk individuals, such as those age 65 years and older, vaccination rates are lower than optimal (less than 70%). Less than 20% of 18–49 year old Americans were ever vaccinated between 1997 and 2002.[31]

Additional measures that could reduce inappropriate care of patients suffering from only a viral infection is increased laboratory testing of pathogens and dissemination of local surveillance data to community-based physicians. A recent prospective randomized controlled trial of rapid diagnostic testing of pediatric patients seen in the emergency room found that once physicians were aware their patients had influenza, antibiotic use decreased, prescriptions for antiviral products increased, and both costs and length of stay were reduced.[32] Two-pronged comprehensive and systematic efforts aimed at (1) prevention of influenza, and (2) accurate diagnostic confirmation of influenza have the potential to dramatically reduce antibiotic misuse.

Acknowledgements

We would like to recognize the following individuals for their contributions to this work: Wyndolyn Bell, MD, Marnie Boron, PharmD, Deborah Charsha-May, PhD, Alan Cohen, MD, FAAP, Robert Fuentes, PharmD, Vincent Haynes, MD, Paulina Kaptur, PhD, Kimmie Kohlhase, MS, and Doris Makari, MD.

This work was presented at the 43rd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy on September 16, 2003, in Chicago, IL.

Conflicts of Interest

All authors of this paper are employees of MedImmune, Inc. MedImmune manufactures and markets the influenza vaccine, FluMist™.

References

1. Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. *JAMA* 1997;**278**(11):901–4.
2. Nyquist AC, Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for children with colds, upper respiratory tract infections, and bronchitis. *JAMA* 1998;**279**(11):875–7.
3. Arnold SR, Allen UD, Al-Zahrani M, Tan DH, Wang EE. Antibiotic prescribing by pediatricians for respiratory tract infection in children. *Clin Infect Dis* 1999;**29**(2):312–7.
4. Kunin CM. Resistance to antimicrobial drugs: a worldwide calamity. *Ann Intern Med* 1993;**118**:557–61.
5. Neu HC. The crisis in antibiotic resistance. *Science* 1992;**257**:1064–73.
6. Swartz MN. Use of antimicrobial agents and drug resistance. *N Engl J Med* 1997;**337**:491–2.
7. Gonzales R, Malone DC, Maselli JH, Sande MA. Excessive antibiotic use for acute respiratory infections in the United States. *Clin Infect Dis* 2001;**33**(6):757–62.
8. Cantrell R, Young AF, Martin BC. Antibiotic prescribing in ambulatory care settings for adults with colds, upper respiratory tract infections, and bronchitis. *Clin Ther* 2002;**24**(1):170–82.
9. Halasa NB, Griffin MR, Zhu Y, Edwards KM. Decreased number of antibiotic prescriptions in office-based settings from 1993 to 1999 in children less than five years of age. *Pediatr Infect Dis J* 2002;**21**(11):1023–8.
10. Nash DR, Harman J, Wald ER, Kelleher KJ. Antibiotic prescribing by primary care physicians for children with upper respiratory tract infections. *Arch Pediatr Adolesc Med* 2002;**156**(11):1114–9.
11. McCaig LF, Besser RE, Hughes JM. Trends in antimicrobial prescribing rates for children and adolescents. *JAMA* 2002;**287**(23):3096–102.
12. Steinman MA, Gonzales R, Lindner JA, Landefeld CS. Changing use of antibiotics in community-based outpatient practice, 1991–1999. *Annals Int Med* 2003;**138**:525–33.
13. Monto AS, Gravenstein S, Elliott M, Colopy M, Schweinle J. Clinical signs and symptoms predicting influenza infection. *Arch Intern Med* 2000;**160**(21):3243–7.
14. Centers for Disease Control and Prevention. Using live, attenuate influenza vaccine for prevention and control of influenza; supplemental recommendations of the advisory committee on immunization practices (ACIP). *MMWR Morb Mortal Wkly Rep* 2003;52(RR13):1–8.
15. Tompkins L, Siller A. Analyzing complex sample survey data: a new beginning. *Proceedings of the SAS User Group, International Conference (SUGI)*. Indianapolis, IN, April 9–12, Paper 238-25.
16. Schappert SM. Ambulatory care visits to physician offices, hospital outpatients departments, and emergency departments: United states, 1997. National Center for Health Statistics. *Vital Health Stat* 1999;**13**(143):1–37.

17. PDR Electronic Library®, *Thompson MICROMEDEX*, Greenwood Village, Colorado (Edition expires [31 December 2003]).
18. Red Book™ for Windows®, *Thompson MICROMEDEX*, Greenwood Village, Colorado (Edition expires [30 April 2003]).
19. Centers for Disease Control and Prevention. Resistance of Streptococcus pneumoniae to fluroquinolones—United States, 1995–1999. MMWR Morb Mortal Wkly Rep. 2001; 50:800–804.
20. Hyde TB, Gay K, Stephens DS, Vugia DJ, Pass M, Johnson S, et al. Macrolide resistance among invasive Streptococcus pneumoniae isolates. *JAMA* 2001;**286**:1857–62.
21. Gupta K, Scholes D, Stamm WE. Increasing prevalence of antimicrobial resistance among uropathogens causing acute uncomplicated cystitis in women. *JAMA* 1999;**281**:736–8.
22. Dowell SF, Schwartz B. Resistant pneumococci: protecting patients through judicious use of antibiotics. *Am Fam Physician* 1997;**55**:1647–54.
23. Dowell SC, Marcy SM, Phillips WR, et al. Principles of judicious use of antimicrobial agents for pediatric upper respiratory tract infections. *Pediatrics* 1998;**101**:163–84.
24. Chen DK, McGeer A, de Azvedo JC, Low DE. Decreased susceptibility of *Streptococcus pneumoniae* to fluoroquinolones in Canada. Canadian Bacterial Surveillance Network. *N Engl J Med* 1999;**341**:233–9.
25. Calvo-Sánchez AJ, Gińon-González JA, López-Prieto D, Canueto-Quintero J, Sánchez-Porto A, Vergara-Campos A, et al. Multivariate analysis of risk factors for infection due to penicillin-resistant and multidrug-resistant *Streptococcus pneumoniae*: a multicenter study. *Clin Infect Dis* 1997; **24**:1052–9.
26. Doern GV. Antimicrobial use and the emergence of antimicrobial resistance with *Streptococcus pneumoniae* in the United States. *Clin Infect Dis* 2001;**33**(Suppl 3): S187–92.
27. Monto AS. The role of antivirals in the control of influenza. *Vaccine* 2003;**21**(16):1796–800.
28. Cox F, Khan ZM, Schweinte JE, Okamotos L, McLaughlin T. Cost associated with the treatment of influenza in a managed care setting. Medscape General Medicine 2000. (http://www.medscape.com. Accessed 2/26/2003.)
29. Lautenbach E, Larosa LA, Kasbekar N, Peng HP, Maniglia RJ, Fishman NO. Fluroquinolone utilization in the emergency departments of academic medical centers. *Arch Intern Med* 2003;**163**:601–5.
30. Berg JS, Dischler J, Wagner DJ, Raia JJ, Palmer-Shevlin N. Medication compliance: a health care problem. *Ann Pharmacother* 1993;**27**(Suppl 9):S1–24.
31. National Center for Health Statistics, Centers for Disease Control and Prevention, National Health Interview Survey, Data tables for Figures. 4.1–4.3. (http://www.cdc.gov/nchs/about/major/nhis/released200209/figures04_1-4_3.htm. Accessed 2/11/2003).
32. Bonner AB, Monroe KW, Talley LI, Klasner AE, Kimberlin DW. Impact of the rapid diagnosis of influenza on physician decision-making and patient management in the pediatric emergency department: results of a randomized, prospective, controlled trial. *Pediatrics* 2003;**112**:363–7.